Clinical Management of Intravesical Drug-Releasing Systems in the Treatment of Bladder Cancer: Considerations Based on Expert Panel Recommendations

Information provided below was developed based on expert urologic experiences. There are no available studies or analyses on the effectiveness of these recommendations. These recommendations are not included in any intravesical drug releasing systems (iDRS) USPI or IFU (see page 3 for more information). These recommendations should not override the HCPs' decision-making, which should consider clinical judgment, patient history, AE experience, and institutional guidelines where applicable for symptom and side effect management of iDRS use.

International Expert Panel (n=17)

An international (US, Europe, China, and Japan) expert panel was convened to develop consensus recommendations on the management of side effects associated with iDRS treatment

- **7** Urologists and urologic oncologists with iDRS experience in the sponsor's (Johnson & Johnson) clinical trials
- **2** Functional urologists
- **8** Physicians and clinical scientist affiliates of the sponsor (Johnson & Johnson)

General Principles and Prophylactic Measures to Consider Based on Clinical Judgement

Counsel on potential lower urinary tract symptoms (LUTS) prior to initiation and throughout the treatment course, and **screen for pre-existing LUTS**

Advise patients to **consume ≥1500 mL (~6.5 cups) of liquid each day** during the iDRS dosing period

Consider counseling patients to avoid bladder irritants (e.g., spicy foods, citrus fruits) if they have ongoing LUTS or history of LUTS prior to treatment

LUTS

Dysuria in the absence of UTI

1. Consider continuing iDRS treatment while initiating symptom management
2. If no clinical improvement, consider removing iDRS/delaying insertion of a new iDRS after removal
3. After complete resolution, iDRS treatment may be resumed based on clinical judgement

Overactive bladder (OAB)*

Steps 1–3 may be followed as listed for dysuria

1. If OAB symptoms persist despite symptom management and a negative culture result, consider cystoscopy to evaluate the degree of mucosal irritation†

Bladder pain associated with OAB

Steps 1–3 may be followed as listed for dysuria

1. Consider the WHO three-step analgesic ladder, with the potential addition of antispasmodics and/or phenazopyridine‡

UTI

UTIs

1. Initiate appropriate antibiotics based on urinalysis and urine culture results
2. Consider leaving iDRS in the bladder through antimicrobial treatment to avoid instrumentation and risks of seeding infection
3. If signs and symptoms worsen despite 48–72 hours of treatment, use clinical judgement to decide whether to remove the iDRS and whether to delay insertion of a replacement iDRS until clinical improvement

Urosepsis

1. Remove iDRS as soon as patient is clinically stable following initiation of broad-spectrum antibiotics
2. After complete resolution of the infection, iDRS treatment may be resumed based on clinical judgement

Hematuria

Macroscopic¶

1. Consider continuing iDRS treatment, while initiating therapy to target cause
2. If no clinical improvement, consider removing iDRS/delaying insertion of a new iDRS after removal
3. If persistent, consider cystoscopy to evaluate presence/recurrence of bladder tumor

Complicated§

1. Consider removing iDRS
2. Consider management of other symptoms (i.e., anemia, obstruction) as clinically indicated, including invasive intervention
3. After complete resolution, iDRS treatment may be resumed based on clinical judgement

*OAB symptoms include micturition urgency, pollakiuria, urge incontinence, and/or nocturia, and/or bladder pain. †To treat mucosal irritation, HCPs could consider a short course of corticosteroids. ‡Step 1 initially and step 2 for persistent pain. ¶Defined as with no clots, no signs of retention, and negative urine culture. §Defined as with clots leading to retention, and/or dysuria or hematuria with anemia.

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Considerations for iDRS Clinical Management Based on Expert Panel Recommendations

Information provided below was developed based on expert urologic experiences (urologists/urologic oncologists from iDRS clinical trials, functional urologists, physicians, and clinical scientists). There are no available studies or analyses on the effectiveness of these recommendations. These recommendations are not included in any intravesical drug releasing systems (iDRS) USPI or IFU (see page 3 for more information). These recommendations should not override the HCPs' decision-making, which should consider clinical judgment, patient history, AE experience, and institutional guidelines where applicable for symptom and side effect management of iDRS use.

Consider counseling patients from treatment initiation on LUTS (storage symptoms), especially males with pre-exisiting symptoms based on IPSS

Symptoms

Urinalysis/urine culture

Adequate hydration

UTI

YES — **Fever** — NO

YES — **Life threatening** — NO

Urosepsis

Consider broad-spectrum antibiotics in accordance with institutional guidance, tailor to antibiogram

UTI with fever

Consider broad-spectrum antibiotics in accordance with institutional guidance, tailor to antibiogram

UTI without fever

Consider culture-directed antibiotics in accordance with institutional guidance

Pain — **OAB**

YES — **Painful urination** — NO

Dysuria

Suggest avoiding irritants

Consider:

- α-blocker
- Antispasmodics
- Phenazopyridine
- NSAIDs
- Amitriptyline, low dose

Abdominal pain, lower

Consider excluding other causes of abdominal pain

Consider step 1 of the WHO three-step analgesic ladder (non-opioid analgesics such as NSAID or acetaminophen)

Consider adding:

- Phenazopyridine and/or
- Antispasmodic

For persistent pain, consider step 2 of the WHO three-step analgesic ladder (weak opioids)

OAB

Suggest avoiding irritants

Consider distraction techniques, bladder retraining, and/or pelvic floor muscle training

Consider anticholinergic drugs or beta-3 agonist in the absence of contraindications

Consider adding LUTS treatment (α blocker, 5α-reductase inhibitor, or PDE-5 inhibitor)

Consider PTNS

Clinically stable?

After 48–72 hours

Clinical improvement?

When deciding whether to remove or continue iDRS, HCPs are advised to apply their clinical judgment with each case. Please refer to Pradere et al. (2025) for additional information from this expert panel, including iDRS management.

Adapted with permission from Pradere B, et al. *Curr Opin Urol*. 2025. doi:10.1097/MOU.0000000000001350.

Scan QR code or go to tago.ca/pradere2025 for more information. See the full manuscript: Pradere B, Schuit M, Guerrero-Ramos F, et al. Side effect management andprocedural best practices with indwelling intravesical drug-releasing systems in the treatment of bladder cancer: recommendations from expert panels. *Curr Opin Urol*. 2025. doi:10.1097/MOU.0000000000001350.

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INLEXZO™ (gemcitabine intravesical system) INDICATION AND SAFETY INFORMATION SUMMARY

Indication

INLEXZO™ is indicated for the treatment of adult patients with Bacillus Calmette-Guérin (BCG)-unresponsive, non-muscle invasive bladder cancer (NMIBC) with carcinoma *in situ* (CIS), with or without papillary tumors.

Contraindications

INLEXZO™ is contraindicated in patients with:

- Perforation of the bladder.
- Prior hypersensitivity reactions to gemcitabine or any component of the product.

Warnings and Precautions

Risks in Patients with Perforated Bladder

INLEXZO™ may lead to systemic exposure to gemcitabine and to severe adverse reactions if administered to patients with a perforated bladder or to those in whom the integrity of the bladder mucosa has been compromised.

Evaluate the bladder before the intravesical administration of INLEXZO™ and do not administer to patients with a perforated bladder or mucosal compromise until bladder integrity has been restored.

Risk of Metastatic Bladder Cancer

Delaying cystectomy in patients with BCG-unresponsive CIS could lead to development of muscle invasive or metastatic bladder cancer, which can be lethal. The risk of developing muscle invasive or metastatic bladder cancer increases the longer cystectomy is delayed in the presence of persisting CIS.

Of the 83 evaluable patients with BCG-unresponsive CIS treated with INLEXZO™ in Cohort 2 of SunRISe-1, 7 patients (8%) progressed to muscle invasive (T2 or greater) bladder cancer. Three patients (3.5%) had progression determined at the time of cystectomy. The median time between determination of persistent or recurrent CIS or T1 and progression to muscle invasive disease was 94 days.

Magnetic Resonance Imaging (MRI) Safety

INLEXZO™ can only be safely scanned with MRI under certain conditions. Refer to section 5.3 of the USPI for details on conditions.

Embryo-Fetal Toxicity

Based on animal data and its mechanism of action, INLEXZO™ can cause fetal harm when administered to a pregnant woman if systemic exposure occurs. In animal reproduction studies, systemic administration of gemcitabine was teratogenic, embryotoxic, and fetotoxic in mice and rabbits.

Advise pregnant women and females of reproductive potential of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment and for 6 months after final removal of INLEXZO™. Advise male patients with female partners of reproductive potential to use effective contraception during treatment and for 3 months after final removal of INLEXZO™.

Adverse Reactions

Serious adverse reactions occurred in 24% of patients receiving INLEXZO™. Serious adverse reactions that occurred in >2% of patients included urinary tract infection, hematuria, pneumonia, and urinary tract pain. Fatal adverse reactions occurred in 1.2% of patients who received INLEXZO™, including cognitive disorder.

The most common (>15%) adverse reactions, including laboratory abnormalities, were urinary frequency, urinary tract infection, dysuria, micturition urgency, decreased hemoglobin, increased lipase, urinary tract pain, decreased lymphocytes, hematuria, increased creatinine, increased potassium, increased AST, decreased sodium, bladder irritation, and increased ALT.

Use in Specific Populations

Pregnancy

There are no available data on the use of INLEXZO™ in pregnant women to inform a drug-associated risk. Please see Embryo-Fetal Toxicity for risk information related to pregnancy.

Lactation

Because of the potential for serious adverse reactions in breastfed infants, advise women not to breastfeed during treatment and for 1 week after final removal of INLEXZO™.

Females and Males of Reproductive Potential

Pregnancy Testing - Verify pregnancy status in females of reproductive potential prior to initiating INLEXZO™.

Contraception - Please see Embryo-Fetal Toxicity for information regarding contraception.

Infertility (Males) - Based on animal studies, INLEXZO™ may impair fertility in males of reproductive potential. It is not known whether these effects on fertility are reversible.

Geriatric Use

Of the patients given INLEXZO™ monotherapy in Cohort 2 of SunRISe-1, 72% were 65 years of age or older and 34% were 75 years or older. There were insufficient numbers of patients <65 years of age to determine if these patients respond differently to patients 65 years of age and older.

AE, adverse event; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BCG, Bacillus Calmette-Guérin; CIS, carcinoma *in situ*; HCP, healthcare professional; iDRS, intravesical drug-releasing systems; IFU, Instructions for Use; IPSS, International Prostate System Score; LUTS, lower urinary tract symptoms; MRI, magnetic resonance imaging; NMIBC, non-muscle invasive bladder cancer; NSAIDs, nonsteroidal anti-inflammatory drugs; OAB, overactive bladder; PDE-5, phosphodiesterase-5; PTNS, percutaneous tibial nerve stimulation; USPI, United States Prescribing Information; UTI, urinary tract infection; WHO, World Health Organization.

Pradere B, et al. *Curr Opin Urol*. 2025. doi:10.1097/MOU.0000000000001350.

Scan QR code or click here to read the full Prescribing Information for INLEXZO™

Scan QR code or click here to read the Instructions for Use for INLEXZO™

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